Reconstruction of kidney renal clear cell carcinoma evolution across pathological stages

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Supplementary Table 1: KIRC sample size of separate stages

Stage	Stage I	Stage II	Stage III	Stage IV	Total
Patients	196	41	113	67	417

Supplementary Table 2: Likelihood test of SMGs distribution in separate stages (Logistic regression)

Gene	p-value(Likelihood)
PBRM1	0.3204
BAP1	0.0062
VHL	0.0285
SETD2	0.0691
TTN	0.1376
MUC4	0.0793
KDM5C	0.9838
MTOR	0.2877

Supplementary Table 3: Survival outcome of known driver genes

Gene	Stage	p-value(log-rank)
VHL	1	0.827
PBRM1	1	0.114
MUC4	1	0.0482
TTN	1	0.893
SETD2	1	0.484
MTOR	1	0.517
KDM5C	1	0.103
BAP1	1	0.281
VHL	2	0.012
PBRM1	2	0.371
MUC4	2	0.161
TTN	2	0.511
SETD2	2	0.0851
MTOR	2	0.585
KDM5C	2	0.0975
BAP1	2	0.807
VHL	3	0.655
PBRM1	3	0.317
MUC4	3	0.0277
TTN	3	0.396
SETD2	3	0.49
MTOR	3	0.899

KDM5C	3	0.144
BAP1	3	0.345
VHL	4	0.914
PBRM1	4	0.265
MUC4	4	0.372
TTN	4	0.215
SETD2	4	0.251
MTOR	4	0.827
KDM5C	4	0.909
BAP1	4	0.196
VHL	all	0.918
PBRM1	all	0.373
MUC4	all	0.0179
TTN	all	0.945
SETD2	all	0.271
MTOR	all	0.316
KDM5C	all	0.0586
BAP1	all	0.101

Supplementary Table 4: Degree of KIRC evolution DAG

Gene	In-degree	Out-degree	In-degree(weighted)	Out-degree(weighted)
ARID1A	1	1	31	20
BAP1	1	1	13	15
DNAH14	1	0	4	0
DNHD1	1	0	10	0
FLG	1	0	5	0
HMCN1	1	1	18	10
KMT2D	1	0	11	0
MTOR	1	0	4	0
MUC16	2	1	22	5
MUC4	5	9	155	101
PBRM1	5	7	183	86
PCLO	2	0	20	0
PDZD2	1	0	10	0
PHF7	2	0	30	0
PRUNE2	2	0	19	0
RRS1	1	0	13	0
RYR2	1	1	14	10
SDK1	1	0	10	0
SETD2	3	0	25	0
SMG1P7	2	2	36	26

TTN	5	1	92	7
VHL	1	19	10	485
WNK1	2	0	30	0
FMN2	0	1	0	5

Supplementary Table 5: Survival outcome of trunk genes

Gene	Stage	p-value(log-rank)
ARID1A	1	0.956
WNK1	1	1.26E-11
DNAH14	1	0.609
DNHD1	1	0.758
FLG	1	0.443
FMN2	1	0.145
PRUNE2	1	0.867
RRS1	1	0.781
RYR2	1	0.611
SDK1	1	0.262
PCLO	1	0.304
PDZD2	1	0.684
HMCN1	1	0.0596
KMT2D	1	0.855
MUC16	1	0.192
PHF7	1	0.671
SMG1P7	1	0.973
ARID1A	2	0.845
WNK1	2	0.382
DNAH14	2	0.629
DNHD1	2	0.000404
FLG	2	0.409
RRS1	2	0.25
RYR2	2	6.95E-07
SDK1	2	0.343
PCLO	2	0.402
HMCN1	2	0.929
PHF7	2	0.487
SMG1P7	2	0.982
ARID1A	3	0.261
DNAH14	3	0.738
DNHD1	3	0.298
FLG	3	0.539
FMN2	3	0.451
RYR2	3	0.696

SDK1	3	0.808
PCLO	3	0.214
PDZD2	3	0.24
HMCN1	3	0.0398
KMT2D	3	0.264
MUC16	3	0.043
PHF7	3	0.457
SMG1P7	3	0.254
ARID1A	4	0.856
DNAH14	4	0.903
DNHD1	4	0.31
FLG	4	0.721
FMN2	4	0.0724
PRUNE2	4	0.113
RYR2	4	0.721
SDK1	4	0.548
PCLO	4	0.000191
PDZD2	4	0.756
HMCN1	4	0.136
KMT2D	4	0.939
MUC16	4	0.535
PHF7	4	0.79
SMG1P7	4	0.702
ARID1A	all	0.398
WNK1	all	0.32
DNAH14	all	0.592
DNHD1	all	0.0383
FLG	all	0.785
FMN2	all	0.501
PRUNE2	all	0.599
RRS1	all	0.958
RYR2	all	0.321
SDK1	all	0.199
PCLO	all	0.211
PDZD2	all	0.904
HMCN1	all	0.286
KMT2D	all	0.202
MUC16	all	0.322
PHF7	all	0.545
SMG1P7	all	0.324

Supplementary Table 6: UCSC database enrichment

stage	gene	PPI_enriched_gene	ratio
1	5	3	0.6
2	6	126	21
3	20	153	7.65
4	35	136	3.885714286

Supplementary Table 7: Edges weight larger than 3 after bootstrap

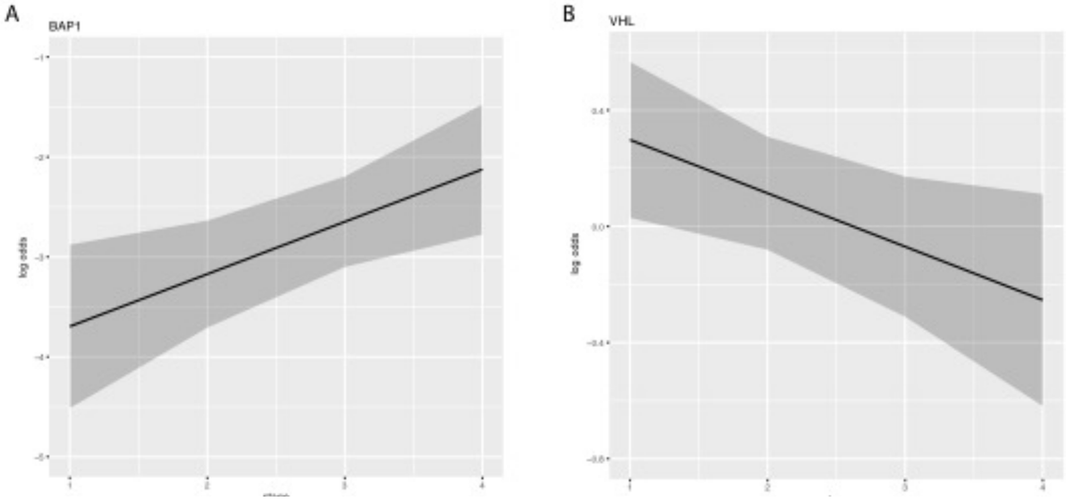
edgeList0	Stage1	Stage2	Stage3	Stage4
VHL,PBRM1	62	26	59	26
VHL,TTN	34	12	10	3
VHL,MUC4	30	8	48	44
PBRM1,TTN	19	4	4	0
PBRM1,MUC4	13	1	20	9
VHL,MUC16	12	0	3	0
PBRM1,MUC16	10	0	3	2
VHL,RYR1	8	0	0	0
TTN,USH2A	7	0	1	0
VHL,KDM5C	6	0	1	0
PBRM1,SMG1P7	6	0	5	0
PBRM1,SETD2	6	4	10	6
MUC16,PRUNE2	5	0	0	0
VHL,SMG1P7	5	2	2	0
VHL,FMN2	5	0	0	1
VHL,SETD2	5	2	7	11
PBRM1,MUC6	4	2	0	0
FMN2,NFAT5	4	0	0	0
HSPA8,SPECC1	4	0	0	0
PBRM1,HSPA8	4	0	0	0
PBRM1,PDE4DIP	4	0	0	0
PBRM1,PRG4	4	0	0	0
VHL,PCNT	4	0	0	0
VHL,CSMD3	4	0	1	0
VHL,SSPO	4	0	1	0
PBRM1,LRP2	4	0	2	0
PBRM1,KDM5C	4	0	1	4
VHL,MTOR	4	0	0	5
PBRM1,VHL	3	4	4	10
MUC4,PBRM1	2	1	6	10
MUC4,TTN	2	2	6	17
VHL,HMCN1	1	17	0	0
MUC4,PCLO	1	15	0	0

VHL,RYR2	1	14	0	0
MUC4,FLG	1	4	0	0
VHL,KMT2C	1	0	4	0
VHL,KMT2D	1	0	10	0
MUC4,SMG1P7	1	21	1	3
PBRM1,SYNE2	1	0	0	5
VHL,DST	1	0	0	5
VHL,PDZD2	1	0	0	10
VHL,ARID1A	0	31	0	0
ARID1A,WNK1	0	20	0	0
BAP1,SMG1P7	0	15	0	0
SMG1P7,BAP1	0	13	0	0
SMG1P7,RRS1	0	13	0	0
HMCN1,SDK1	0	10	0	0
RYR2,DNHD1	0	10	0	0
VHL,WNK1	0	10	0	0
COL1A2,NOTCH2	0	9	0	0
PBRM1,MEGF6	0	9	0	0
SETD2,PDE4DIP	0	9	0	0
TTN,IGF2R	0	9	0	0
ADAMTS12,FCGBP	0	8	0	0
ARID1A,TRPC4	0	8	0	0
HMCN1,OBSL1	0	8	0	0
PBRM1,CDAN1	0	8	0	0
PBRM1,COL1A2	0	8	0	0
PDE4DIP,PRDM2	0	8	0	0
AHNAK2,DNAH9	0	7	0	0
MUC6,ZMYM2	0	7	0	0
SETD2,NCOA6	0	7	0	0
ARID1A,GOLGA5	0	6	0	0
COL1A2,RBM28	0	6	0	0
MUC4,MAST4	0	6	0	0
MUC6,EPPK1	0	6	0	0
NCOA6,PDE4DIP	0	6	0	0
PBRM1,ATP13A4	0	6	0	0
PCLO,ATP8A1	0	6	0	0
PCLO,MTMR11	0	6	0	0
SETD2,DMXL2	0	6	0	0
SETD2,MTOR	0	6	0	0
VHL,SDK1	0	6	0	0
BAP1,PREX1	0	5	0	0
BIRC6,AIDA	0	5	0	0

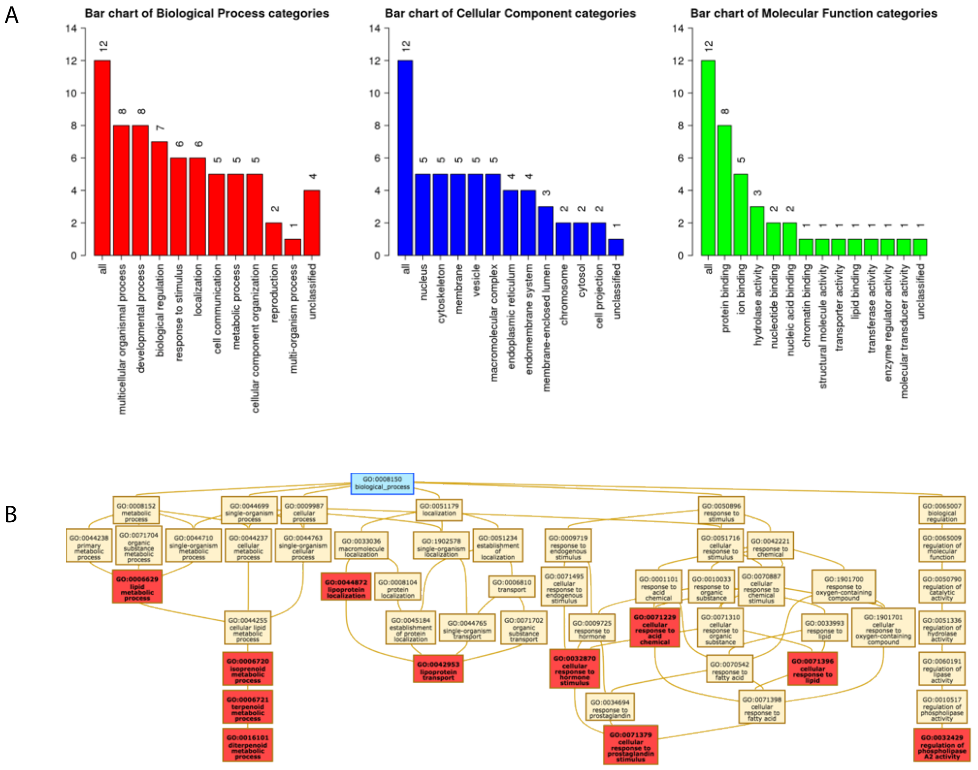
HMCN1,TTN	0	5	0	0
MUC4,GUCY1A3	0	5	0	0
MUC4,HRC	0	5	0	0
MUC4,RBM23	0	5	0	0
MUC6,CCDC74A	0	5	0	0
PBRM1,11-Sep	0	5	0	0
PCLO,SETD2	0	5	0	0
SETD2,CNTRL	0	5	0	0
TTN,NXPE2	0	5	0	0
WNK1,ARID1A	0	5	0	0
ABCC5,ATM	0	4	0	0
ADAMTS12,ODF2	0	4	0	0
COL1A2,CACNA1D	0	4	0	0
ITGA11,ZNF594	0	4	0	0
MUC4,GPR179	0	4	0	0
MUC4,KIAA2018	0	4	0	0
MUC4,PCK1	0	4	0	0
MUC6,MYLK3	0	4	0	0
MUC6,PER2	0	4	0	0
MUC6,VPS13A	0	4	0	0
NNT,EPHX1	0	4	0	0
NOTCH2,RBM28	0	4	0	0
PBRM1,COL5A3	0	4	0	0
PBRM1,GBF1	0	4	0	0
SETD2,PCLO	0	4	0	0
SETD2,PRDM2	0	4	0	0
TTN,ERCC1	0	4	0	0
TTN,RFTN1	0	4	0	0
TTN,TNRC6B	0	4	0	0
VHL,BDH2	0	4	0	0
VHL,CEP68	0	4	0	0
TTN,BRWD1	0	7	1	0
SMG1P7,NEFH	0	6	1	0
MUC4,VHL	0	5	1	0
MUC4,BAP1	0	8	3	0
MUC4,DNAH14	0	0	4	0
MUC4,FAT3	0	0	4	0
PBRM1,GLG1	0	0	4	0
PBRM1,RTTN	0	0	4	0
PKHD1L1,FOXD1	0	0	4	0
KMT2D,USH2A	0	0	5	0
MUC16,PTEN	0	0	5	0

MUC4,KMT2D	0	0	5	0
PBRM1,THSD7B	0	0	5	0
PBRM1,ZFHX4	0	0	5	0
VHL,BAP1	0	5	6	0
MUC4,USH2A	0	0	6	0
PBRM1,EGFR	0	0	6	0
PBRM1,KMT2C	0	0	7	0
PBRM1,SLC22A9	0	0	7	0
MUC4,MUC6	0	4	0	1
MUC4,SETD2	0	2	4	2
MTOR,SYNE2	0	0	0	4
PBRM1,FREM2	0	0	0	4
PBRM1,MTOR	0	0	0	4
TTN,DMBT1	0	0	0	4
VHL,FAM153A	0	0	0	4
DST,CROCC	0	0	0	5
PBRM1,SYNJ2	0	0	0	5
SYNE1,CACNA1C	0	0	0	5
SYNE1,KMT2C	0	0	0	5
SYNE2,UBR4	0	0	0	5
PBRM1,PHF7	0	0	1	5
VHL,DMKN	0	0	1	5
PBRM1,MED12L	0	0	0	6
PHF7,MUC5B	0	0	0	6
MUC4,DNMT1	0	0	0	7
MUC4,PHF7	0	0	0	11
MUC4,PRUNE2	0	0	0	14
VHL,PHF7	0	0	0	19

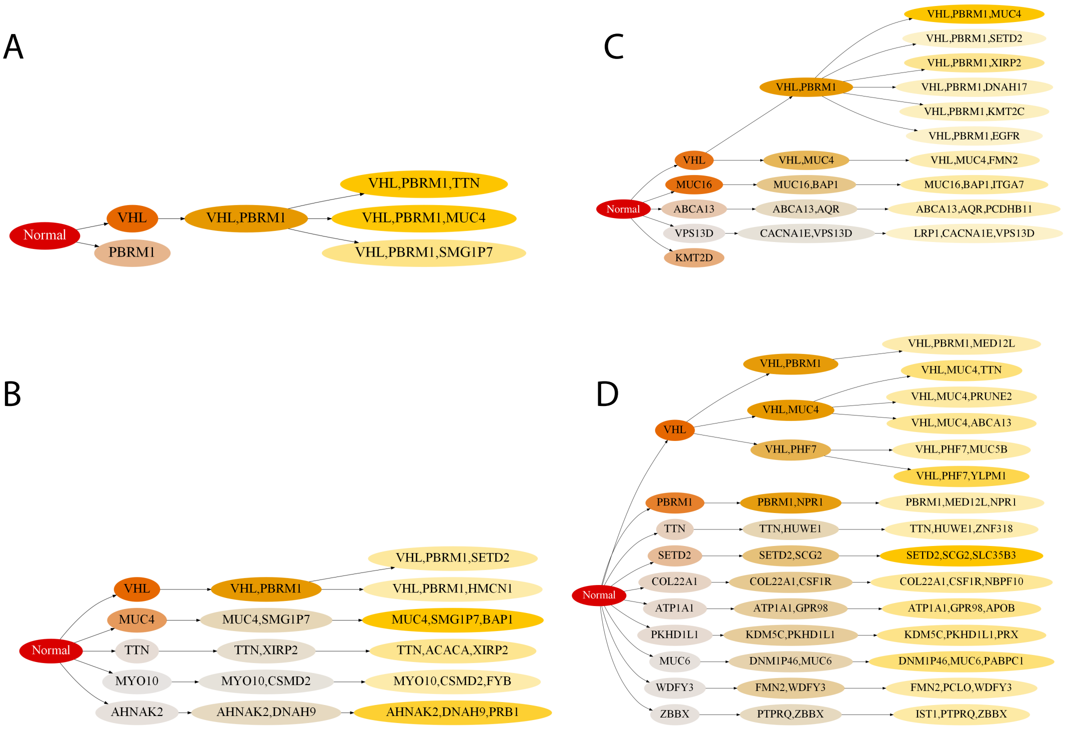
Supplementary Fig 1: Logistic regression model of mutation and stage



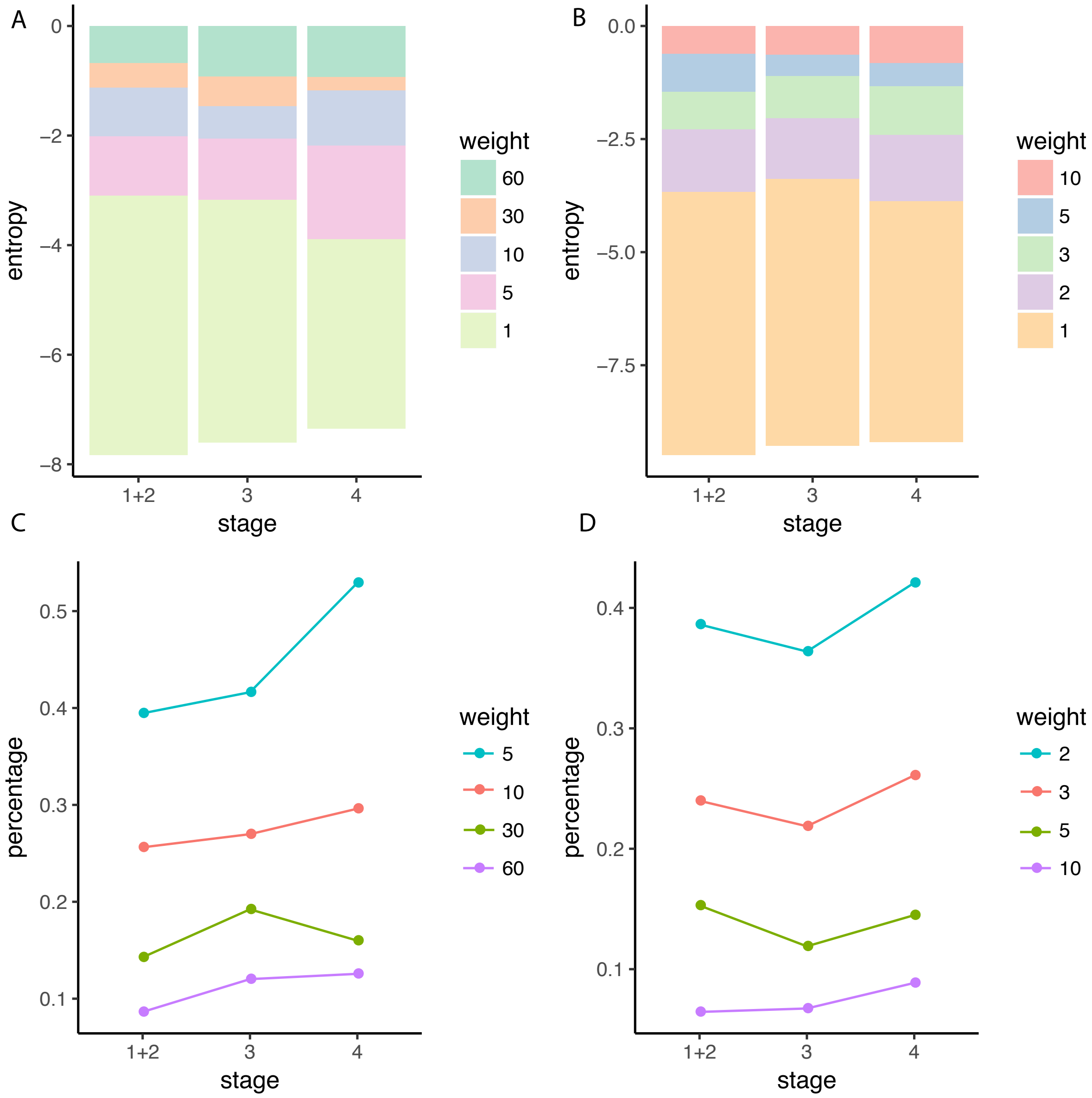
Supplementary Figure 2: Function enrichment of trunk genes. (A) GO slim. (B) GO database.



Supplementary Figure 3: Evolution DAG separate stages of raw data



Supplementary Figure 4: Entropy distribution of high bootstrap score nodes and edges. (A) Nodes' entropy. (B) Edges' entropy. (C) Percentage of high bootstrap score nodes in total entropy. (D) Percentage of high bootstrap score edges in total entropy.



Supplementary Figure 5: PCLO stage IV expression survival curve (with low FMN2 expression)